

### ***Amendments***

#### ***In the Specification:***

On page 1, line 4, before "Description of Background Art," please insert the following:

#### **Cross-Reference to Related Applications**

This application is a divisional of Appl. No. 09/947,387, filed September 7, 2001, allowed, which is a division of Appl. No. 09/168,888, filed October 9, 1998, now U.S. Pat. No. 6,342,611, which claims the benefit of U.S. Prov. Appl. No. 60/145,746, filed March 3, 1998, abandoned, and U.S. Prov. Appl. No. 60/061,582, filed October 10, 1997, abandoned, all of which are wholly incorporated by reference herein.

#### ***In the Claims:***

Please cancel claims 1-90 without prejudice or disclaimer.

Please add the following new claims:

91. (new) A method to determine the sensitivity of an animal with cancer to treatment with one or more chemotherapeutic agents, comprising

(a) contacting cancer cells taken from said animal with said one or more chemotherapeutic agents and a reporter compound having the Formula II:



or the Formula V:



or a biologically acceptable salt of said compound or a tautomer of said compound or a biologically acceptable salt of said tautomer, wherein:

$R_1$  is an *N*-terminal protecting group;

each AA independently is a residue of an  $\alpha$ -amino acid or  $\beta$ -amino acid, or a methyl, acetoxymethyl or methoxy ester of a carboxyl-containing  $\alpha$ -amino acid or  $\beta$ -amino acid;

each  $n$  independently is 0-5;

$y$  is a fluorogenic or fluorescent moiety; and

$R_6$  is a blocking group which is not an amino acid or a derivative of an amino acid;

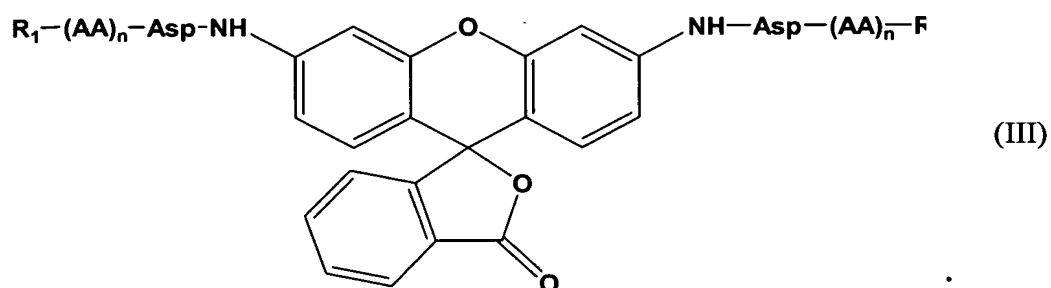
under conditions whereby said one or more agents, either interacts with an external receptor or is taken into said cancer cells, and

(b) recording the fluorescence of said cancer cells compared to control cells which have only been contacted with said reporter compound, wherein a change in fluorescence of said cancer cells compared to said control cells is an indication that said cancer cells are chemosensitive to said one or more chemotherapeutic agents and that said animal is sensitive to said treatment.

92. (new) The method of claim 91, wherein  $R_6$  is a blocking group which is selected from the group consisting of  $C_{1-12}$ alkyloxycarbonyl,  $CH_3(OCH_2CH_2)_qOCO-$ ,  $CH_3(CH_2)_r(OCH_2CH_2)_sOCO-$ ,  $C_{1-12}(\text{alkylthio})\text{carbonyl}$ , aryl( $C_{1-12}$ )alkoxycarbonyl,  $H_2NCO-$ ,  $(CH_3)_2NCO-$ ,  $(CH_3CH_2)_2NCO-$ ,  $(CH_3(CH_2)_v)(CH_3)NCO-$ ,  $C_{1-12}$ alkylsulfonyl,  $C_{1-12}$ haloalkylsulfonyl, aryl( $C_{1-12}$ )alkylsulfonyl,  $Cl_3CCH_2OCO-$ , unsubstituted benzoyl, benzylcarbonyl, phenylsulfonyl and tosyl; wherein  $q$  is 2-4,  $r$  is 0-5,  $s$  is 1-4, and  $v$  is 1-9.

93. (new) The method of claim 91, wherein (AA)<sub>n</sub>-Asp is selected from the group consisting of HD, AD, TD, VD, LD, PD, ND, ED, YD, ID, EHD, VAD, ETD, EVD, HVD, ELD, GPD, EPD, GTD, LND, EED, SLD, VPD, EAD, SYD, LPD, EID, WEHD SEQ ID NO:1, YVAD SEQ ID NO:2, LEHD SEQ ID NO:3, DETD SEQ ID NO:4, DEVD SEQ ID NO:5, DEHD SEQ ID NO:6, VEHD SEQ ID NO:7, LETD SEQ ID NO:8, LEVD SEQ ID NO:9, SHVD SEQ ID NO:10, DELD SEQ ID NO:11, DGPD SEQ ID NO:12, DEPD SEQ ID NO:13, DGTD SEQ ID NO:14, DLND SEQ ID NO:15, DEED SEQ ID NO:16, DSLD SEQ ID NO:17, DVPD SEQ ID NO:18, DEAD SEQ ID NO:19, DSYD SEQ ID NO:20, ELPD SEQ ID NO:21, VEID SEQ ID NO:26, IETD SEQ ID NO:24, IEPD SEQ ID NO:23 and VEPD SEQ ID NO:27.

94. (new) The method of claim 91, wherein said compound is of formula III:



95. (new) The method of claim 94, wherein said compound is selected from the group consisting of:

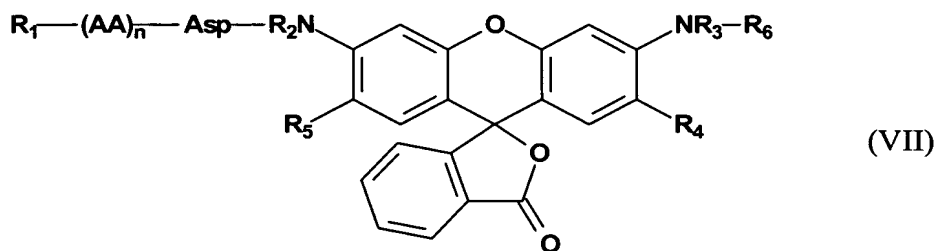
(Z-YVAD)<sub>2</sub>-Rhodamine 110, SEQ ID NO:2;

(Z-DEVD)<sub>2</sub>-Rhodamine 110, SEQ ID NO:5;

(Z-VAD)<sub>2</sub>-Rhodamine 110;

(Z-YVAD(OAM))<sub>2</sub>-Rhodamine 110, SEQ ID NO:2;  
(Z-LE(OAM)HD(OAM))<sub>2</sub>-Rhodamine 110, SEQ ID NO:3;  
(Z-D(OAM)E(OAM)TD(OAM))<sub>2</sub>-Rhodamine 110, SEQ ID NO:4;  
(Z-D(OAM)E(OAM)VD(OAM))<sub>2</sub>-Rhodamine 110, SEQ ID NO:5;  
(Z-D(OMe)E(OMe)VD(OAM))<sub>2</sub>-Rhodamine 110, SEQ ID NO:5; and  
(Z-D(OMe)E(OMe)VD)<sub>2</sub>-Rhodamine 110 SEQ IS NO:5.

96. (new) The method of claim 91, wherein said compound is of formula VII:



wherein R<sub>2</sub> and R<sub>3</sub> independently are hydrogen, methyl or ethyl.

97. (new) The compound of claim 96, wherein R<sub>1</sub> is t-butyloxycarbonyl, acetyl, hexanoyl, octanoyl or benzyloxycarbonyl; and R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are hydrogen.

98. (new) The method of claim 96, wherein said compound is selected from the group consisting of:

*N*-(Z-YVAD)-*N'*-acetyl-Rhodamine 110, SEQ ID NO:2;  
*N*-(Z-DEVD)-*N'*-acetyl-Rhodamine 110, SEQ ID NO:5;  
*N*-(Z-VD)-*N'*-acetyl-Rhodamine 110;  
*N*-(Z-AD)-*N'*-acetyl-Rhodamine 110;

*N*-(Z-VAD)-*N*'-acetyl-Rhodamine 110;

*N*-(Z-DEVD)-*N*'-ethoxycarbonyl-Rhodamine 110, SEQ ID NO:5;

*N*-(Ac-DEVD)-*N*'-ethoxycarbonyl-Rhodamine 110, SEQ ID NO:5;

*N*-(Ac-DEVD)-*N*'-hexyloxycarbonyl-Rhodamine 110, SEQ ID NO:5;

*N*-(Ac-DEVD)-*N*'-octyloxycarbonyl-Rhodamine 110, SEQ ID NO:5;

*N*-(Ac-DEVD)-*N*'-decyloxycarbonyl-Rhodamine 110, SEQ ID NO:5;

*N*-(Ac-DEVD)-*N*'-dodecyloxycarbonyl-Rhodamine 110, SEQ ID NO:5; and

*N*-(Ac-DEVD)-*N*'-(ethylthio)carbonyl-Rhodamine 110, SEQ ID NO:5;

wherein Z is benzyloxycarbonyl.

99. (new) The method of claim 91, wherein said animal is a human.

100. (new) A method for monitoring the treatment of an animal to treatment with one or more chemotherapeutic agents, comprising

- (a) administering said one or more chemotherapeutic agents to said animal,
- (b) contacting cells taken from said animal after said administering with a

reporter compound having the Formula II:



or the Formula V:



or a biologically acceptable salt of said compound or a tautomer of said compound or a biologically acceptable salt of said tautomer, wherein:

$R_1$  is an *N*-terminal protecting group;

each AA independently is a residue of an  $\alpha$ -amino acid or  $\beta$ -amino acid, or a methyl, acetoxymethyl or methoxy ester of a carboxyl-containing  $\alpha$ -amino acid or  $\beta$ -amino acid;

each n independently is 0-5;

y is a fluorogenic or fluorescent moiety; and

R<sub>6</sub> is a blocking group which is not an amino acid or a derivative of an amino acid;

under conditions whereby said reporter compound is taken into said cells, and

(c) recording the fluorescence of said cells contacted with said reporter compound compared to control cells which have been taken from said animal before said administering,

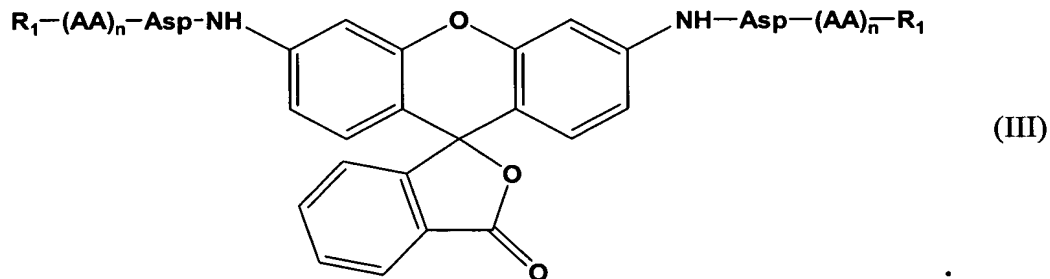
wherein a change in fluorescence of said cells taken from said animal compared to said control cells is an indication that said animal is sensitive to said chemotherapeutic agents.

101. (new) The method of claim 100, wherein R<sub>6</sub> is a blocking group which is selected from the group consisting of C<sub>1-12</sub>alkyloxycarbonyl, CH<sub>3</sub>(OCH<sub>2</sub>CH<sub>2</sub>)<sub>q</sub>OCO-, CH<sub>3</sub>(CH<sub>2</sub>)<sub>r</sub>(OCH<sub>2</sub>CH<sub>2</sub>)<sub>s</sub>OCO-, C<sub>1-12</sub>(alkylthio)carbonyl, aryl(C<sub>1-12</sub>)alkoxycarbonyl, H<sub>2</sub>NCO-, (CH<sub>3</sub>)<sub>2</sub>NCO-, (CH<sub>3</sub>CH<sub>2</sub>)<sub>2</sub>NCO-, (CH<sub>3</sub>(CH<sub>2</sub>)<sub>v</sub>)(CH<sub>3</sub>)NCO-, C<sub>1-12</sub>alkylsulfonyl, C<sub>1-12</sub>haloalkylsulfonyl, aryl(C<sub>1-12</sub>)alkylsulfonyl, Cl<sub>3</sub>CCH<sub>2</sub>OCO-, unsubstituted benzoyl, benzylcarbonyl, phenylsulfonyl and tosyl; wherein q is 2-4, r is 0-5, s is 1-4, and v is 1-9.

102. (new) The method of claim 100, wherein (AA)<sub>n</sub>-Asp is selected from the group consisting of HD, AD, TD, VD, LD, PD, ND, ED, YD, ID, EHD, VAD, ETD,

EVD, HVD, ELD, GPD, EPD, GTD, LND, EED, SLD, VPD, EAD, SYD, LPD, EID, WEHD SEQ ID NO:1, YVAD SEQ ID NO:2, LEHD SEQ ID NO:3, DETD SEQ ID NO:4, DEVD SEQ ID NO:5, DEHD SEQ ID NO:6, VEHD SEQ ID NO:7, LETD SEQ ID NO:8, LEVD SEQ ID NO:9, SHVD SEQ ID NO:10, DELD SEQ ID NO:11, DGPD SEQ ID NO:12, DEPD SEQ ID NO:13, DGTD SEQ ID NO:14, DLND SEQ ID NO:15, DEED SEQ ID NO:16, DSLD SEQ ID NO:17, DVPD SEQ ID NO:18, DEAD SEQ ID NO:19, DSYD SEQ ID NO:20, ELPD SEQ ID NO:21, VEID SEQ ID NO:26, IETD SEQ ID NO:24, IEPD SEQ ID NO:23 and VEPD SEQ ID NO:27.

103. (new) The method of claim 100, wherein said compound is of formula III:

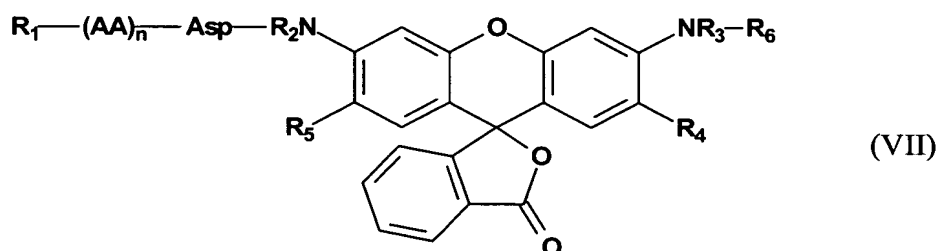


104. (new) The method of claim 103, wherein said compound is selected from the group consisting of:

- (Z-YVAD)<sub>2</sub>-Rhodamine 110, SEQ ID NO:2;
- (Z-DEVD)<sub>2</sub>-Rhodamine 110, SEQ ID NO:5;
- (Z-VAD)<sub>2</sub>-Rhodamine 110;
- (Z-YVAD(OAM))<sub>2</sub>-Rhodamine 110, SEQ ID NO:2;
- (Z-LE(OAM)HD(OAM))<sub>2</sub>-Rhodamine 110, SEQ ID NO:3;

(Z-D(OAM)E(OAM)TD(OAM))<sub>2</sub>-Rhodamine 110, SEQ ID NO:4;  
(Z-D(OAM)E(OAM)VD(OAM))<sub>2</sub>-Rhodamine 110, SEQ ID NO:5;  
(Z-D(OMe)E(OMe)VD(OAM))<sub>2</sub>-Rhodamine 110, SEQ ID NO:5; and  
(Z-D(OMe)E(OMe)VD)<sub>2</sub>-Rhodamine 110 SEQ IS NO:5.

105. (new) The method of claim 100, wherein said compound is of formula VII:



wherein R<sub>2</sub> and R<sub>3</sub> independently are hydrogen, methyl or ethyl.

106. (new) The compound of claim 105, wherein R<sub>1</sub> is t-butyloxycarbonyl, acetyl, hexanoyl, octanoyl or benzyloxycarbonyl; and R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are hydrogen.

107. (new) The method of claim 105, wherein said compound is selected from the group consisting of:

*N*-(Z-YVAD)-*N*'-acetyl-Rhodamine 110, SEQ ID NO:2;  
*N*-(Z-DEVD)-*N*'-acetyl-Rhodamine 110, SEQ ID NO:5;  
*N*-(Z-VD)-*N*'-acetyl-Rhodamine 110;  
*N*-(Z-AD)-*N*'-acetyl-Rhodamine 110;  
*N*-(Z-VAD)-*N*'-acetyl-Rhodamine 110;



*N*-(Z-DEVD)-*N*'-ethoxycarbonyl-Rhodamine 110, SEQ ID NO:5;  
*N*-(Ac-DEVD)-*N*'-ethoxycarbonyl-Rhodamine 110, SEQ ID NO:5;  
*N*-(Ac-DEVD)-*N*'-hexyloxycarbonyl-Rhodamine 110, SEQ ID NO:5;  
*N*-(Ac-DEVD)-*N*'-octyloxycarbonyl-Rhodamine 110, SEQ ID NO:5;  
*N*-(Ac-DEVD)-*N*'-decyloxycarbonyl-Rhodamine 110, SEQ ID NO:5;  
*N*-(Ac-DEVD)-*N*'-dodecyloxycarbonyl-Rhodamine 110, SEQ ID NO:5; and  
*N*-(Ac-DEVD)-*N*'-(ethylthio)carbonyl-Rhodamine 110, SEQ ID NO:5;

wherein Z is benzyloxycarbonyl.

108. (new) The method according to claim 100, wherein said animal suffers from a malady related to apoptotic cell death.

***In the Sequence Listing:***

After the claims, please insert pages 1-40 of the Sequence Listing filed concurrently herewith.